Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01 MAY 2006	**N/A**	**-**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Damage control resuscitation: the need for specific blood products to treat the coagulopathy of trauma	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
Hess J. R., Holcomb J. B., Hoyt D. B.,	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT NUMBER
United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX 78234	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**SAR**	**2**	

Damage control resuscitation: the need for specific blood products to treat the coagulopathy of trauma

Civilian trauma centers and military combat support hospitals have evolved to treat increasingly severe injury.[1] Today, they routinely save patients whose care would have been futile two decades ago. The most important advance has been an approach called "damage control" surgery in which the restoration of normal anatomy is deferred to limit the progression of coagulopathy.[2] This technique has been developed to the point that it has outstripped conventional blood bank support. Uncontrolled coagulopathic hemorrhage is now the major cause of potentially preventable death following trauma.

Roughly 1 in 10 people in the United States is brought to or seeks medical care for injury each year. One in a 100 is hospitalized, and approximately 1 in a 1000 receives blood products as part of the acute treatment of injury. At the University of Maryland Shock-Trauma Center (UMSTC) in calendar year 2000, 8 percent of 5649 injured patients admitted directly from the scene of injury received RBCs during their hospital stay, 5 percent received plasma, 3 percent received PLTs, and 0.1 percent received cryoprecipitate.[3] Eleven percent of all the RBC units were given in the first hour as un–cross-matched group O RBCs; 62 percent of all the RBC units transfused were given in the first 24 hours of care. A total of 143 individuals, 2.3 percent of all those admitted, received more than 10 units of RBCs each, ultimately accounting for 75 percent of the total blood products given. Mortality among those who received transfusions of more than 10 units was 39 percent. In contrast, mortality among those who received 0 to 4 units was 0.6 percent.

Recent military experience confirms the civilian reports of MacLeod and her colleagues[4] and Brohi and his colleagues[5] showing the presence of coagulopathy in the most seriously injured at the time of admission and the association of coagulopathy on admission with poor outcome. In 734 casualties admitted to a US Army combat support hospital (CSH) in Tikrit, Iraq, who received 0 to 4 units of blood, their INR was uniformly normal on admission and mortality was 0.6 percent (M. Schreiber, personal communication). In Baghdad, 243 (5.4%) casualties were massively transfused (>10 units of RBC) and of those with an INR of greater than 1.5 or decreased PLTs on admission, mortality was 30 percent (G. Perkins, personal communication). Those massively transfused with an admission INR of less 1.5 had a mortality of 5 percent. These data are remarkably similar to those from the civilian trauma center in Baltimore.

The recognition that the coagulopathy of trauma is present at the time of admission in the most seriously injured patients is a critical one. It can be identified with modern point-of-care testing, available in most emergency departments. Blood loss, hemodilution by physiologic vascular refill, consumption of PLTs, and coagulation factors on exposed subendothelial cells and matrix proteins, hypothermic PLT dysfunction and reduced enzyme activity, acidosis-induced reductions in coagulation factor complex activity, and unopposed fibrinolysis all contribute to this coagulopathy. In patients with similar injury scores, those presenting with coagulopathy have mortality two to three times greater than patients with normal coagulation values. Contrary to conventional wisdom, this coagulopathy exists before any substantial dilution by standard crystalloid or colloid resuscitation.

Most military and civilian patients (>94%) who present to trauma centers do not have and will not develop coagulopathy. Treating these patients blindly with plasma, PLTs, and cryoprecipitate is both wasteful and dangerous. Seriously injured patients, however, do have a measurable coagulopathy at the time they arrive at the trauma center, and the presence of low PLT counts and prolonged coagulation times at the time of admission are ominous signs. Nevertheless, resuscitation customarily proceeds with crystalloid fluids and plasma-poor RBCs in additive solution (AS), often for many liters and several hours, because these are the products that are immediately available. These products inevitably further dilute coagulation factors and contribute to worsening coagulopathy. Cosgriff and coworkers[6] have shown that as the sum and severity of hypotension, acidosis, hypothermia, and injury severity increase in individual patients, the incidence of coagulopathy approaches 100 percent, and mortality 56 percent.

Unfortunately, the composition and time course of administration of conventional blood products contributes to this negative spiral. ABO typing and the thawing and issuing of type-specific FFP during the initial trauma resuscitation requires time, during which resuscitation without PLTs and coagulation factors continues and the presenting coagulopathy worsens. After liters of fluid, and during the second and third hours of such resuscitation,

TRANSFUSION 2006;46:685-686.

plasma, PLTs, and cryoprecipitate are finally added to the resuscitation regime, but even on a unit-for-unit basis with RBCs, they generally fail to correct coagulopathy in the most severely injured and rapidly bleeding patients. FFP, PLTs, and RBCs in AS are all dilute products and contribute calculably to this outcome.[7] Given the mean composition of units of RBCs in AS, FFP, and apheresis PLTs, the maximum achievable Hct level is 29 percent, coagulation factor activity is 62 percent, and PLT count is about 88×10^9 per L. Actual recoveries of circulating RBCs and PLTs will be 10 and 30 percent lower, respectively.

The ability to control hemorrhage is the critical determinant of outcome in the seriously injured, and trauma research is increasingly focused on new approaches to hemorrhage control after acute injury.[1] Animal studies show that higher concentrations of fibrinogen reduce bleeding.[8,9] Clinical series suggest that higher ratios of PLTs-RBCs administration have the same beneficial effect.[6,10] The clinical results of blinded trauma trials utilizing rFVIIa are suggestive.[11] Several trauma centers are starting to provide thawed AB plasma in the emergency department.

The development, manufacturing, and regulatory support for new product and more readily available current products must come from the blood bank community. Earlier initiation of plasma into the initial trauma resuscitation process will require greater and more widespread inventories of thawed AB plasma. Universal donor group AB thawed plasma for earlier administration will require directed apheresis collection so as not to impinge on the limited availability of this product for infants and AB patients. More concentrated plasma can be made available by freeze-drying single-donor apheresis jumbo units of AB plasma as is practiced by the Belgian Army and the Australian Red Cross. Such units can be reconstituted in less than normal volumes of water to make concentrated plasma to correct coagulopathy and for field hospital and emergency department use. Cryoprecipitate is the only available source of fibrinogen in the United States at this time. Its availability in larger, 6- to 10-unit, prepooled bags would facilitate rapid issue and administration. These new or modified products will provide immediate hemostatic resuscitation of seriously injured patients, rather than the current practice of delay, further dilution, and increased mortality. Blood products that were designed to meet the needs of elective surgery or oncology patients and the needs of the plasma fractionating industry can be improved to meet the needs of severely injured patients. Injury is rapidly becoming the second most common cause of death worldwide. We need blood products to address the coagulopathy of trauma.

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